

diamonds, FIG. 3B) of a cypher family were counted as true mutations (see bottom of FIG. 3B).

**[0078]** Wild-type TP53 Exon 4 sequence was compared to the actual sequence results and substitutions were plotted before (FIG. 4A) and after correction with Cypher Seq (FIG. 4B). Prior to correction, the detected error frequency was  $3.9 \times 10^{-4}$ /bp (FIG. 4A). In short, the initial error frequency reflects assay-related errors (e.g., PCR, sequencing, and other errors introduced after bar-coding). This means that detecting a rare mutation is difficult due to the noise-to-signal ratio being very high. After Cypher Seq correction, however, the error frequency dropped to  $8.8 \times 10^{-7}$ /bp (FIG. 4B). In other words, the remaining substitutions are most likely biological in nature and most likely reflect errors introduced during replication in *E. coli* prior to ligation into

the barcoded vectors. Thus, true mutations (i.e., those that arise naturally in a cell during replication) are readily detectable using the cypher system of the instant disclosure.

**[0079]** The various embodiments described above can be combined to provide further embodiments. All of the U.S. patents, U.S. patent application publications, U.S. patent applications, foreign patents, foreign patent applications and non-patent publications referred to in this specification and/or listed in the Application Data Sheet are incorporated herein by reference, in their entirety. In general, in the following claims, the terms used should not be construed to limit the claims to specific embodiments disclosed in the specification and claims, but should be construed to include all possible embodiments along with the full scope of equivalents to which such claims are entitled. Accordingly, the claims are not limited by the disclosure.

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#### SEQUENCE LISTING

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<210> SEQ ID NO 1  
 <211> LENGTH: 7  
 <212> TYPE: DNA  
 <213> ORGANISM: Artificial Sequence  
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 <223> OTHER INFORMATION: Random cypher sequence  
 <220> FEATURE:  
 <221> NAME/KEY: misc\_feature  
 <222> LOCATION: (1)..(7)  
 <223> OTHER INFORMATION: n = A,T,C or G

<400> SEQUENCE: 1

nnnnnnnn

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<210> SEQ ID NO 2  
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 <223> OTHER INFORMATION: An oligonucleotide containing EcoRI and BamHI restriction enzyme sites, adapter sequences, indices, and random 7-nucleotide barcodes flanking a SmaI restriction enzyme site  
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 <221> NAME/KEY: misc\_feature  
 <222> LOCATION: (1)..(195)  
 <223> OTHER INFORMATION: n = A,T,C or G

<400> SEQUENCE: 2

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ttggaattcg ataca	195

<210> SEQ ID NO 3  
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 <220> FEATURE:  
 <223> OTHER INFORMATION: forward primer sequence

<400> SEQUENCE: 3

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22